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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/709,801	05/28/2004	Caroline Desponts	USF-212XZ1T	2999

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
11/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/709,801	DESPONTS ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 18-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 18-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3-05, 8-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communications filed 8-21-07.

Claims 1, 3, 18-25 are pending in the instant application.

The declaration under 37 CFR 1.132 filed 8-21-07 is insufficient to overcome the rejection of claims 1, 3, 18-25 based upon 35 U.S.C. 112, first paragraph, scope of enablement as set forth in the last Office action for the reasons of record set forth below.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

Claims 1, 3 and 18-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the in vitro reduction of expression of SHIP-1 in ES cells, and being enabling for the in vivo inhibition of SHIP expression in peripheral blood mononuclear cells, thereby increasing Mac+Gr1-monocytes and circulating Mac1+GR1+ cells (myeloid suppressor cells) using siRNA, does not reasonably provide enablement for methods of increasing the yield of stem cells in a patient, which stem cells comprise hematopoietic stem cells, mammary stem cells,

mesenchymal and organ specific stem cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant's arguments and declaration filed 8-21-07 have been fully considered but they are not persuasive. Applicant argues that the full scope is enabled because partial inhibition of expression of SHIP-1 has been achieved in vivo using siRNA (*a.k.a.* RNAi). Applicant argues that the inhibition of expression of SHIP in embryonic stem (ES) cells transfected in vitro has been demonstrated using siRNA. Applicant also argues that the in vivo inhibition of SHIP expression has been shown in peripheral blood mononuclear cells, with a concomitant increase in Mac+Gr1-monocytes and circulating Mac1+GR1+ cells (myeloid suppressor cells) following RNAi inhibition of SHIP-1 in vivo.

The claims, however, are broadly drawn to methods of increasing the yield of any stem cells in a patient, which stem cells optionally comprise hematopoietic stem cells, mammary stem cells, mesenchymal and organ specific stem cells, which methods comprise administration of an RNAi compound that inhibits SHIP expression in a patient, and which methods optionally further comprise harvesting stem cells from the patient, and optionally re-administering the harvested stem cells to the patient.

Contrary to Applicant's assertions, the in vitro inhibition of SHIP-1 in ES cells and the in vivo inhibition of SHIP-1 using RNAi do not enable the full scope of the claimed invention. Applicants have not provided guidance in the specification toward a method of increasing the number of any (and/or all) stem cells in vivo comprising the administration of an RNAi specific for SHIP mRNA. Applicant has shown the inhibition

of expression of SHIP in embryonic stem (ES) cells transfected in vitro using siRNA. Applicant has shown the in vivo inhibition of SHIP expression in peripheral blood mononuclear cells, thereby increasing Mac+Gr1-monocytes and circulating Mac1+GR1+ cells (myeloid suppressor cells) using siRNA.

The ability to inhibit SHIP-1 expression in ES cells in vitro and to inhibit SHIP-1 expression in vivo using siRNA, whereby Mac+Gr1-monocytes and circulating Mac1+GR1+ cells are increased in vivo, are not representative or correlative of the ability to increase the yield of any stem cell in an organism, including hematopoietic stem cells, mammary stem cells, mesenchymal and organ specific stem cells in a patient.

One skilled in the art would not accept on its face the examples given in the specification of in vitro transfections, of biochemical, cellular and immunological characterization of stem and other progenitor cells obtained from mouse ablation models, and increasing Mac+Gr1-monocytes and circulating Mac1+GR1+ cells in vivo following SHIP-1 inhibition using siRNA as being correlative or representative of the ability to increase the yield of this wide array of stem cells (any stem cells) in a subject in a patient. This is in view of the lack of guidance in the specification and known unpredictability associated with the ability to predict an increase in any type of stem cell in vivo. The unpredictability of stem cell expansion and stem cell fate in vitro and in vivo is well known in the art and has been discussed in the following references: Hemmati-Vrivanlou et al, Cell, Vol. 88, pages 13-17, 1997; Bjorklund et al., PNAS, Vol. 99, No. 4,

pages 2344-2349, 2003; Kim et al., Nature, June 20, 2002, pages 1-7; Kawasaki, et al., Neuron, Vol. 28, pages 31-40, 2000.

The breadth of the claims is very broad. The claims are drawn to methods of increasing the yield of any stem cells in a patient, which stem cells optionally comprise hematopoietic stem cells, mammary stem cells, mesenchymal and organ specific stem cells, which methods comprise the administration of an RNAi compound that inhibits SHIP expression in a patient, and which methods optionally further include harvesting stem cells from the patient, and optionally re-administering the harvested stem cells to the patient.

The quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of accessible target sites, modes of delivery and formulations to target appropriate cells and /or tissues harboring the target gene or genes SHIP, whereby SHIP expression is inhibited in vivo, and further whereby any stem cells, including but not limited to hematopoietic stem cells, mammary stem cells, mesenchymal and organ specific stem cells, have increased yields in a patient following the administration, by any means, of an RNAi specific for SHIP mRNA.

Since the specification fails to provide any particular guidance for the successful increase in any (any/or all) stem cells in a patient comprising administration of an RNAi, and since determination of the factors to increase the large genus of stem cells claimed in a patient is highly unpredictable, it would require undue experimentation to practice the invention over the scope claimed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE CO PIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jane Zara whose telephone number is (571) 272-0765. If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, James Douglas Schultz, can be reached on (571) 272-0763. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
11-9-07

JANE ZARA, PH.D.
PRIMARY EXAMINER